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L13: Entry 25 of 349 File: USPT Jul 24, 2001

DOCUMENT-IDENTIFIER: US 6265196 B1
TITLE: Methods for inactivating target DNA and for detecting conformational change in a nucleic acid

DEPR:
Bacteriophages have been shown to be effective in the treatment of experimental E. coli infection (10,11). More recently, bacteriophage was shown to prevent destruction of skin grafts by Pseudomonas aeruginosa (12). These bacteriophages can be engineered to carry the lethal hybrid endonuclease genes targeted against their hosts. These bacteriophages will be more effective in the destruction of the bacteria they infect. The present invention specifically includes this concept as well. The present invention also contemplates the delivery of other normal as well as mutant site-specific restriction enzymes using a similar approach.

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L13: Entry 28 of 349 File: USPT Jul 10, 2001

DOCUMENT-IDENTIFIER: US 6258847 B1
TITLE: Use of 2-mercaptoethanolamine (2-MEA) and related aminothiol compounds and copper(II)-3,5 di-isopropyl salicylates and related compounds in the prevention and treatment of various diseases

DEPR:
Prior art consists of acidophilus, for example, in capsules, chosen for its purity and color, whereas in nature nothing exists like that. Living biological systems described here are unique in a) the combination; b) the number of organisms; c) the location of the organisms. There is no other therapy which seeks to occupy structures other than the intestines, for example, of living biological systems. These can also be inserted as a nasal spray for nasal sinuses and lungs, where a living biological system can comprise viruses, bacteria, fungi, etc. For example, in the immune compromised state, phages for various bacteria can be assembled as a living biological system and inhaled on a daily or weekly basis to prevent infection with said bacteria. The living biological system as described herein may be defined by its constituents or may be defined by the activity of the constituents. For example, a virus, bacteria, fungus and yeast which carry anti-cancer activity could be combined into an anti-cancer living biological system. Living biological systems may exist whole or processed such that they are lysed so that whatever internal enzymatic factors may be released into the system. They can also be formulated to target specific sources and their internal nutrients can do the same, and a living biological system can be formed which would be a constant producer of by-products. For example, organisms which are capable of manufacturing vitamin C can be orally administered once a month and would continue to produce the said vitamin in body for the duration of the month. Living biological systems make it possible to insert replicating forms of enzymes so that it is taken only once a month or once a year.

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L13: Entry 181 of 349 File: USPT Sep 22, 1998

DOCUMENT-IDENTIFIER: US 5811093 A
TITLE: Bacteriophage genotypically modified to delay inactivations by the host defense system

ABPL:
The present invention is directed to bacteriophage therapy, using methods that enable the bacteriophage to delay inactivation by any and all parts of the host defense system (HDS) against foreign objects that would tend to reduce the numbers of bacteriophage and/or the efficiency of those phage at killing the host bacteria in an infection. Disclosed is a method of producing bacteriophage modified for anti-HDS purposes, one method being selection by serial passaging of a bacteriophage, and the other method being genetic engineering of a bacteriophage, so that the modified bacteriophage will remain active in the body for longer periods of time than the wild-type phage.

BSPR:
The present invention relates to a method of delaying the inactivation of bacteriophages by an animal's host defense system. One method of delaying inactivation is the use of novel bacteriophages whose genomes have been modified. Methods useful for modifying the bacteriophage genome include but are not limited to selection of mutant strains by serial passage, and the creation of new strains by genetic engineering. Such novel bacteriophages have the ability to delay being sequestered by, engulfed by, or otherwise inactivated by one or more of the processes of an animal's host defense system (HDS). This novel attribute allows the "anti-HDS modified" bacteriophage to have a longer survival time in an animal's body than the corresponding wild-type bacteriophage, and that in turn allows the modified phage to be more effective than the wild-type phage at treating (or assisting in the treatment of) a bacterial infection.

BSPR:
The present invention also is directed to specific methods of using bacteriophages for treating infectious bacterial diseases. The route of administration can be by any means including delivering the phage by aerosol to the lungs.

BSPR:
In the 1920s, shortly after the discovery of bacterial viruses (bacteriophages), the medical community began to extensively pursue the treatment of bacterial diseases with bacteriophage therapy. The idea of using phage as a therapy for infectious bacterial diseases was first proposed by d'Herelle in 1918, as a logical application of the bacteriophages' known ability to invade and destroy bacteria. Although early reports of bacteriophage therapy were somewhat favorable, with continued clinical usage it became clear that this form of therapy was inconsistent and unpredictable in its results. Disappointment with phage as a means of therapy grew, because the great potential of these viruses

to kill bacteria in vitro was not realized in vivo. This led to a decline in attempts to develop clinical usage of phage therapy, and that decline accelerated once antibiotics began to be introduced in the 1940s and 50s. From the 1960s to the present, some researchers who adopted certain bacteriophages as a laboratory tool and founded the field of molecular biology have speculated as to why phage therapy failed.

BSPR:
Despite the general failure of phage as therapy, isolated groups of physicians have continued to try to use these agents to treat infectious diseases. Many of these efforts have been concentrated in Russia and India, where the high costs of and lack of availability of antibiotics continues to stimulate a search for alternative therapies. See for example Vogovazova et al., "Effectiveness of Klebsiella pneumoniae Bacteriophage in the Treatment of Experimental Klebsiella Infection", Zhurnal Mikrobiologii, Epidemiologii Immunobiologii, pp. 5-8 (April, 1991); and Vogovazova et al., "Immunological Properties and Therapeutic Effectiveness of Preparations of Klebsiella Bacteriophages", Zhurnal Mikrobiologii, Epidemiologii Immunobiologii, pp. 30-33 (March, 1992)!. These articles are similar to most of the studies of phage therapy, including the first reports by d'Herelle, in that they lack many of the controls required by researchers who investigate anti-infectious therapies. In addition, these studies often have little or no quantification of clinical results. For example, in the second of the two Russian articles cited above, the Results section concerning Klebsiella phage therapy states that "Its use was effective in . . . ozena (38 patients), suppuration of the nasal sinus (5 patients) and of the middle ear (4 patients) . . . In all cases a positive clinical effect was achieved without side effects from the administration of the preparation". Unfortunately, there were no placebo controls or antibiotic controls, and no criteria were given for "improvement".

BSPR:
Another clinical use of phage that was developed in the 1950s and is currently still employed, albeit to a limited extent, is the use of phage lysate, specifically staphphage lysate (SPL). The researchers in this field claim that a nonspecific, cell-mediated immune response to staph endotoxin is an integral and essential part of the claimed efficacy of the SPL. [See, eg., Esber et al., J. Immunopharmacol., Vol. 3, No. 1, pp. 79-92 (1981); Aoki et al., Augmenting Agents in Cancer Therapy (Raven, N.Y.), pp. 101-112 (1981); and Mudd et al., Ann. NY Acad. Sci., Vol. 236, pp. 244-251 (1974).] In this treatment, it seems that the purpose of using the phage is to lyse the bacteria specifically to obtain bacterial antigens, in a manner that those authors find preferential to lysing by sonication or other physical/chemical means. Here again, some difficulties arise in assessing these reports in the literature, because, in general, there are no placebo controls and no standard antibiotic controls against which to measure the reported efficacy of the SPL. More significantly, there is no suggestion in these articles to use phage per se in the treatment of bacterial diseases. Moreover, the articles do not suggest that phage should be modified in any manner that would delay the capture/sequestration of phage by the host defense system.

BSPR:
Since many patients will recover spontaneously from infections, studies must have carefully designed controls and explicit criteria to confirm that a new agent is effective. The lack of quantification and of controls in most of the phage reports from d'Herelle on makes it difficult if not impossible to determine if the phage therapies have had any beneficial effect.

BSPR:
Another object of the present invention is to develop a method for treating bacterial infectious diseases in an animal by administering to the animal an effective amount of the novel bacteriophage, and by an appropriate route of administration.

BSPR:

The administration of an anti-HDS phage that has been developed by serial passage or by genetic engineering will enable the animal recipient to efficaciously fight an infection with the corresponding bacterial pathogen. The phage therapy of this invention will therefore be useful either as an adjunct to standard anti-infective therapies, or as a stand-alone therapy.

DRPR:

FIG. 3 shows a comparison of the efficacy of the wild-type .lambda.vir to that of the selected long-circulating strains Argo1 and Argo2, as therapeutic agents for the treatment of bacteremia caused by the IP injection of E. coli CRM1 into Balb/c female mice. All of the mice were injected IP with a lethal dose of E. coli CRM1 (2.times.10.sup.8 colony forming units). Thirty minutes later the mice in group 2 (.box-solid.) received an IP injection if .lambda.vir and the mice in group 3 (.circle-solid.) received an IP injection of Argo1. Mice in group 1 (.tangle-solidup.) did not receive any phage. A fourth group treated with Argo2 produced results indistinguishable from those observed with Argo1. The mice were observed and rated according to their condition for a period of 100 hours: 0=normal mouse; 1=decreased activity and ruffled fur; 2=lethargy, ruffled fur and hunchback posture; 3=lethargy, ruffled fur, hunchback posture and partially closed eyes with exudate around the eyes; 4=moribund; 5=death. As the observations are categorical condition-stage observations, the actual distances between the states is unknown. For this reason, the level of illness indicated in this illustration is provided simply to record the progression of the disease state. In addition, there was no significant variation of symptoms within any of the experimental groups.

DEPR:

One of the major obstacles to bacteriophage therapy is the fact that when phages are administered to animals, they are rapidly eliminated by the animal's HDS. That suggests that the phages are not viable in the animal's circulation or tissues for a long enough time to reach the site of infection and invade the bacteria. Thus, the object of the present invention is to develop bacteriophages that are able to delay inactivation by the HDS. This will prolong phage viability in the body.

DEPR:

Instead of awaiting the spontaneous mutations that are selected for in the above method, alternatively mutations can be provoked during the growth of the phage in its host bacteria. The mutations may produce specimens of phage that, after selection by serial passage, are even more efficient than the non-mutagenized phage at delaying inactivation by the host defense system. Mutagenization is achieved by subjecting the phage to various stimuli, such as, but not limited to, acridine compounds, ethidium bromide in the presence of light, radioactive phosphorus, and various forms of radiation (X-rays, UV light, etc.). Mutants resulting from the iterative procedure described above, and that are found to have a longer survival time than the wild-type phage, are grown to high titer and are used to treat infectious diseases in animals and in humans.

DEPR:

The present invention can be applied across the spectrum of bacterial diseases, either by serial passage of phages (mutagenized or non-mutagenized) or by genetically engineering phages, so that phages are developed that are specific for each of the bacterial strains of interest. In that way, a full array of anti-HDS selected and/or anti-HDS engineered bacteriophage is developed for virtually all the bacterial (and other applicable) pathogens for man, his pets, livestock and zoo animals (whether mammal, avian, or pisciculture). Phage therapy will then be available:

DEPR:

The second embodiment of the present invention is the development of methods to treat bacterial infections in animals through phage therapy with the anti-HDS modified bacteriophages described above. Hundreds of bacteriophages and the bacterial species they infect are known in the art. The present invention is not limited to a specific bacteriophage or a specific bacteria. Rather, the present invention can be utilized to develop anti-HDS modified bacteriophages which can be used to treat any and all infections caused by their host bacteria.

DEPR:
There are additional bacterial pathogens too numerous to mention that, while not currently in the state of antibiotic-resistance crisis, nevertheless make excellent candidates for treatment with anti-HDS modified bacteriophages that are able to delay inactivation by the HDS, in accordance with the present invention. Thus, all bacterial infections caused by bacteria for which there is a corresponding phage can be treated using the present invention.

DEPR:
The anti-HDS modified bacteriophage of the present invention can be used as a stand-alone therapy or as an adjunctive therapy for the treatment of bacterial infections. Numerous antimicrobial agents (including antibiotics and chemotherapeutic agents) are known in the art which would be useful in combination with anti-HDS modified bacteriophage for treating bacterial infections. Examples of suitable antimicrobial agents and the bacterial infections which can be treated with the specified antimicrobial agents are listed below. However, the present invention is not limited to the antimicrobial agents listed below as one skilled in the art could easily determine other antimicrobial agents useful in combination with anti-HDS modified bacteriophage.

DEPR:
Determination that the anti-HDS selected phage has a greater capacity than wild-type phage to prevent lethal infections in mice.

DEPR:
Determination that the genetically engineered phage has a greater capacity than wild type phage to prevent lethal infections in mice.

DEPR:
Determination that anti-HDS selected phage specific for two types of bacteria have a greater capacity to prevent lethal infections than the wild type phage.

DEPR:
Four groups of mice were injected IP with 2.times.10.sup.8 cfu of E. coli CRM1. The mice were scored for degree of illness as previously described. The first group was a control, with no phage treatment. Within 5 hours these mice exhibited ruffled fur, lethargy and hunchback posture. By 24 hours they were moribund, and they died within 48 hours. There were three groups treated with phage. All of the mice treated with phage survived. However, those treated with .lambda.vir (Group 2) had severe illness before finally recovering, while those treated with Argo1 (Group 3) and Argo2 (Group 4) exhibited only minor signs of illness before complete recovery (FIG. 2).

DEPR:
The following results show that the ability of phage to influence bacterial infections is dose-dependent. Mice were injected IP with CRM1 (2.times.10.sup.8 cfu) suspended in PBS and stored overnight. In contrast to the experiment in FIG. 2, the control group that did not receive any phage in this experiment did not die by 48 hours, an effect that was likely due to reduced virulence of the

washed and refrigerated bacteria used in this experiment. However, they did develop moderately severe signs of illness. In the phage treatment groups, 30 minutes after the bacterial injection the animals received Argo1 phage in doses ranging from 10.sup.2 to 10.sup.10 pfu. As shown in FIG. 3, at the minimum doses of phage (10.sup.2 pfu), at 30 hours after infection, the animals show illness which was only slightly reduced from that seen in the controls. With increasing doses of phage, the animals fared progressively better. At the maximum dose of phage used (10.sup.10 pfu), the animals showed only minimal illness (decreased physical activity and ruffled fur), and these animals were nearly fully recovered at 48 hours.

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L13: Entry 199 of 349 File: USPT Apr 21, 1998

DOCUMENT-IDENTIFIER: US 5741697 A
TITLE: Bacteriophage of chlamydia psittaci

DEPR:
The isolation of .phi.CPG1 and the subsequent molecular cloning of its DNA have important short and long term implications for Chlamydia research. The particular significance of .phi.CPG1 is that, for the first time, a vector for the introduction of foreign DNA into a mammalian Chlamydia is available. In general, four broad categories for the use of such a bacteriophage- or bacteriophage DNA-based system of genetic transfer are: (1) the development of Chlamydia vaccines, (2) the development of diagnostic tests for chlamydial infections, (3) the development of tools to study the epidemiology of chlamydial infections, and (4) the development of therapeutic reagents and therapeutic strategies against chlamydial infections of humans and animals.

DEPR:
The study of the bacteriophage interaction with the Chlamydia cell may also provide a direct means of therapeutic intervention. Since the bacteriophage causes a lytic infection of Chlamydia cells, it should "attenuate" the chlamydial infection (i.e., reduce the infectious load) of eukaryotic cells. Moreover, the virulence of the bacteriophage toward Chlamydia could also be enhanced (e.g. by selecting or screening for more infectious phages). Treatment of other bacterial infections with lyric bacteriophages has been attempted in other systems with little success. However, the containment of chlamydial infections within defined anatomical sites that are readily accessible to external treatment (e.g. the conjunctiva or the genital tract) may render bacteriophage treatment of chlamydial infections possible. In this case, a bacteriophage suspension may be inoculated in the appropriate site in order to infect and lyse the infecting chlamydiae. Such a treatment may entirely eliminate the chlamydial infection or alternatively reduce its magnitude, thereby eliminating or reducing associated morbidity.

DEPR:
Alternatively, bacteriophage components may competitively inhibit chlamydial adherence to or entry into susceptible eukaryotic cells thereby blocking chlamydial infection. Thus, the study of the phage biology itself and of its interaction with the host chlamydial cell may lead to the development of new bacteriophage-derived therapies which may directly inhibit, attenuate or suppress chlamydial infectivity. In this case, bacteriophage-derived peptides or proteins may be effective as therapeutic agents by blocking the specific interaction(s) between eukaryotic receptors and their chlamydial ligands which are normally used by chlamydial elementary bodies to gain entry into the eukaryotic cell.

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L13: Entry 295 of 349 File: USPT Sep 18, 1990

DOCUMENT-IDENTIFIER: US 4957686 A
TITLE: Use of bacteriophages to inhibit dental caries

DEPR:
This invention relates to a method of preventing dental caries by using phages parasitic to the S. Sanguis bacteria, either alone or in conjunction with a mixture of phages containing such variety as to contain phages which attack S. Mutans, Lactobaccilii and any other bacteria which may cause caries or gum disease, to reduce the receptor sites of S. Sanguis on the tooth surface for such acid forming bacterial colonisation.

DEPR:
Using the methods of the invention by regularly placing in the mouth phages parasitic to S. Sanguis and thus preventing the build up of plaque, there is no way that concentrations of other bacteria can be formed which concentrations over time would have led to periodontoses, gingivitis and pyorrhea. Thus the methods of the invention are protective of these dental diseases as well as dental caries. The methods of this invention are primarily to destroy by bacteriophages those bacteria which are not harmful themselves but which facilitate colonisation of tooth surfaces by providing receptor sites to which harmful bacteria can adhere.

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L13: Entry 333 of 349 File: USPT Jul 10, 1984

DOCUMENT-IDENTIFIER: US 4458630 A
TITLE: Disease control in avian species by embryonal vaccination

BSPR:
Taylor et al. (U.S. Pat. No. 2,851,006) teaches a method for increasing the hatch rate of bacterially infected eggs by means of in ovo treatment with a suitable bacteriophage. The phage is introduced to the interior of the egg prior to incubation by any of a variety of techniques including hypodermic syringe, pressure differential in a dipping fluid, and jet spray. By virtue of this technique, disease agents present in the extraembryonic membranes and fluids can be controlled by direct action of the inoculant. In U.S. Pat. No. 3,120,834, Goldhaft et al. expands the application taught in Taylor to a variety of substances including antibiotics, sulfonamides, vitamins, enzymes, nutrients, and inorganic salts. These agents in a liquid carrier are introduced through the shell prior to incubation by means of vacuum impregnation. Nicely et al. (U.S. Pat. No. 3,256,856) offers an improvement to the method of Goldhaft et al. in providing one or more holes in the egg shell for facilitating penetration. The hole is made in the air cell end of the egg, not extending beyond the inner shell membrane. The commercial practicality of the vacuum impregnation technique is limited by the unreliability of obtaining a uniform treatment and the economic unfeasibility of charging the dipping vats with expensive vaccines.

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L4: Entry 27 of 34 File: USPT May 9, 1989

DOCUMENT-IDENTIFIER: US 4828999 A
TITLE: Bacteriophage prevention and control of harmful plant bacteria

CLPR:
1. A method of preventing or controlling bacterial harm to plants by a particular species of a harmful bacterium to which the plants are susceptable, comprising applying to the plants, to seed from which the plants are produced, or to the soil in which the plants are grown, a bacteriophage composition containing a mixture of different phages specific for said species of harmful bacterium, said mixture including at least one viral h mutant specific for at least one phage resistant mutant of the particular species of harmful bacterium.

CLPR:
6. A bacteriophage composition for preventing or controlling bacterial harm to plants by a particular species of a harmful bacterium, said composition comprising a mixture of different phages specific for said species of harmful bacterium, said mixture including at least one viral h mutant specific for at least one phage resistant mutant of the particular species of harmful bacterium.

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Search Results - Record(s) 1 through 13 of 13 returned.

1. Document ID: US 6130221 A

L1: Entry 1 of 13 File: USPT Oct 10, 2000

DOCUMENT-IDENTIFIER: US 6130221 A
TITLE: Pharmaceutical agents that impede the initiation and progression of primary and secondary DMS disruptions

INZZ:
Ghanbari; Hossein

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw. Desc	Image

2. Document ID: US 6121036 A

L1: Entry 2 of 13 File: USPT Sep 19, 2000

DOCUMENT-IDENTIFIER: US 6121036 A
TITLE: Compositions containing bacteriophages and methods of using bacteriophages to treat infections

INZZ:
Ghanbari; Hossein A.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw. Desc	Image

3. Document ID: US 5982100 A

L1: Entry 3 of 13 File: USPT Nov 9, 1999

DOCUMENT-IDENTIFIER: US 5982100 A
TITLE: Inductively coupled plasma reactor

INZZ:
Ghanbari; Ebrahim

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image

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☐ 4. Document ID: US 5916392 A

L1: Entry 4 of 13 File: USPT Jun 29, 1999

DOCUMENT-IDENTIFIER: US 5916392 A
TITLE: Method of application and composition of coating for building surfaces

INZZ:
Ghanbari; Manouchehr M.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Draw Desc	Image

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☐ 5. Document ID: US 5811310 A

L1: Entry 5 of 13 File: USPT Sep 22, 1998

DOCUMENT-IDENTIFIER: US 5811310 A
TITLE: The Alz-50 monoclonal antibody and diagnostic assay for alzheimer's disease

INZZ:
Ghanbari; Hossein A.

Full	Title	Citation	Front	Review	Classification	Date	Reference	KWIC	Draw Desc	Image

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☐ 6. Document ID: US 5556521 A

L1: Entry 6 of 13 File: USPT Sep 17, 1996

DOCUMENT-IDENTIFIER: US 5556521 A
TITLE: Sputter etching apparatus with plasma source having a dielectric pocket and contoured plasma source

INZZ:
Ghanbari; Ebrahim

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 5455197 A

L1: Entry 7 of 13 File: USPT Oct 3, 1995

DOCUMENT-IDENTIFIER: US 5455197 A
TITLE: Control of the crystal orientation dependent properties of a film deposited on a semiconductor wafer

INZZ:
Ghanbari; Abe

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

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☐ 8. Document ID: US 5429947 A

L1: Entry 8 of 13 File: USPT Jul 4, 1995

DOCUMENT-IDENTIFIER: US 5429947 A
TITLE: Diagnosing Alzheimer's disease and schizophrenia

INZZ:
Ghanbari; Hossein A.

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

9. Document ID: US 5418571 A

L1: Entry 9 of 13 File: USPT May 23, 1995

DOCUMENT-IDENTIFIER: US 5418571 A
TITLE: Decoding of double layer video signals with interpolation replacement on missing data from enhancement layer

INZZ:
Ghanbari; Mohammed

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

10. Document ID: US 5280219 A

L1: Entry 10 of 13 File: USPT Jan 18, 1994

DOCUMENT-IDENTIFIER: US 5280219 A
TITLE: Cluster tool soft etch module and ECR plasma generator therefor

INZZ:
Ghanbari; Ebrahim

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

11. Document ID: US 5105007 A

L1: Entry 11 of 13 File: USPT Apr 14, 1992

DOCUMENT-IDENTIFIER: US 5105007 A
TITLE: Phenylacetylglutamine (PAG) analytical test

INZZ:
Ghanbari; Hossein A.

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

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☐ 12. Document ID: US 5100807 A

L1: Entry 12 of 13 File: USPT Mar 31, 1992

DOCUMENT-IDENTIFIER: US 5100807 A
TITLE: Phenylacetylglutamine (PAG) analytical test

INZZ:
Ghanbari; Hossein A.

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

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☐ 13. Document ID: US 4778561 A

L1: Entry 13 of 13 File: USPT Oct 18, 1988

DOCUMENT-IDENTIFIER: US 4778561 A
TITLE: Electron cyclotron resonance plasma source

INZZ:
Ghanbari; Ebrahim

Full | Title | Citation | Front | Review | Classification | Date | Reference | KWIC | Draw Desc | Image

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Terms	Documents
ghanbari.in.	13

Display 50 Documents, starting with Document: 13

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